CASE REPORT

Multifocal metastatic spread of gestational trophoblastic neoplasia: a rare case of uterine choriocarcinoma with pulmonary, vaginal, hepatic, splenic, and renal involvement

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ABSTRACT

Gestational Trophoblastic Neoplasia (GTN) presents various trophoblastic tissue abnormalities, from benign hydatidiform mole to malignant choriocarcinoma. Here, we report a rare case of a 26-year-old woman with a history of three consecutive early gestational miscarriages. Symptoms included vaginal bleeding, dyspnoea, and abdominal pain. Radiological findings showed widespread metastasis to the lungs, vagina, liver, spleen, and kidneys, indicating aggressive choriocarcinoma. Biopsy confirmed the diagnosis, revealing highly atypical trophoblastic cells with extensive vascular invasion. Despite aggressive treatment involving chemotherapy, surgical resection, and supportive care, the patient's prognosis remains guarded, with persistent metastases. This case underscores the complexity of managing advanced GTN with multifocal metastases, requiring a tailored multidisciplinary approach. It also emphasizes the importance of suspecting GTN in women with recurrent miscarriages for timely intervention and improved outcomes.

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INTRODUCTION

Gestational Trophoblastic Neoplasia (GTN) encompasses a spectrum of gestational disorders characterized by abnormal proliferation of trophoblastic cells following abnormal fertilization events. Among these, choriocarcinoma represents the most malignant form, marked by rapid growth and propensity for early hematogenous spread to distant sites. While GTN is relatively rare, its clinical manifestations can vary widely, posing diagnostic and therapeutic challenges.

The incidence of GTN is estimated to be approximately 1 in 1500 pregnancies, with choriocarcinoma comprising approximately 1-2% of all gestational trophoblastic diseases [1]. Despite its rarity, GTN carries significant morbidity and mortality, particularly when diagnosed at an advanced stage with widespread metastatic involvement. In the context of our case, the patient's history of three consecutive miscarriages raises suspicion for underlying gestational trophoblastic pathology, prompting further investigation.

Recurrent miscarriages have been identified as a potential risk factor for GTN, suggesting a shared pathophysiological basis related to abnormal trophoblastic proliferation [2]. Trophoblasts, specialized cells of the placenta, play a critical role in implantation and early embryonic development. Dysregulation of trophoblast function can lead to various gestational disorders, including molar pregnancies and choriocarcinoma. Studies have implicated genetic, hormonal, and environmental factors in the aetiology of GTN, highlighting the complex interplay between host and environmental determinants [3].

The diagnosis of GTN relies on a combination of clinical, radiological, and histopathological findings. Clinical presentation may include abnormal uterine bleeding, pelvic pain, respiratory symptoms, and features of metastatic disease. Radiological imaging, such as ultrasound and computed tomography (CT), is instrumental in assessing tumour extent and identifying

metastatic sites. In our case, imaging studies revealed widespread metastases involving multiple organs, indicative of advanced disease.

Histopathological examination of tissue specimens remains the gold standard for confirming the diagnosis of GTN. Choriocarcinoma is characterized by malignant trophoblastic cells with high mitotic activity and frequent vascular invasion. In our case, histopathological analysis of biopsy samples confirmed the presence of choriocarcinoma, corroborating the clinical suspicion. Herein, we present a unique case of GTN in a 26-year-old female with a history of recurrent miscarriages, demonstrating multifocal metastatic spread and emphasizes the importance of early recognition and intervention.

CASE PRESENTATION

A 26-year-old multigravida (G4P1L1A3) presented to the emergency department with a complex clinical presentation marked by a two-month history of abnormal vaginal bleeding, dyspnoea, and generalised abdominal discomfort. Her obstetric history revealed a pattern of recurrent miscarriages, totalling three consecutive losses in the early gestational period (5-6 weeks of gestation) over the past three years. She reported irregular menstrual cycles and recent onset amenorrhoea, raising suspicion for underlying gestational trophoblastic pathology. Upon examination, the patient appeared visibly pale and fatigued, with signs of tachypnoea and tachycardia. Gynaecological assessment revealed active vaginal bleeding, alongside an enlarged, tender uterus with irregular contour corresponding to 8-10 weeks upon bimanual examination, indicative of possible uterine pathology. Laboratory investigations unveiled severe anaemia and thrombocytopenia, alongside derangements in liver and renal function tests. Markedly elevated serum beta-human chorionic gonadotropin (β-HCG) levels (150,000 mIU/mL) further supported the suspicion of trophoblastic disease. Radiological imaging through contrast-enhanced computed tomography (CECT) delineated a grim scenario, showcasing a fairly defined mixed-dense lesion located within the myometrium of the fundus of the uterus, measuring approximately 6.6 x 8.5 x 9.5 cm, causing contour bulge and effacing the zonal anatomy of the uterine parenchyma (Fig . 1 A/B), post-contrast imaging of this lesion highlights peripheral intensely enhancing serpiginous features with central non-enhancement during the arterial phase, followed by washout during subsequent venous and delayed phases. Moreover, there are multiple engorged, and tortuous enhancing Para uterine/gonadal vessels, along with focal enhancing nodular thickening affecting the anterior wall of the vagina, indenting the posterior wall of the urinary bladder, with compressed fat planes suggestive of vaginal extension of the lesion (Fig – 1 B). Additionally, there are no internal calcifications or fat components detected, and perilesional or retroperitoneal lymphadenopathy is absent.

Furthermore, the examination reveals multiple hypodense lesions within the spleen, which exhibit peripheral enhancement and central non-enhancement during the arterial phase, followed by washout in subsequent venous and delayed phases giving a possibility of splenic metastasis (Fig – 2 A/B). Additionally, both the kidneys exhibit multiple iso - dense and mildly hyperdense lesions involving both cortical and medullary regions, these lesions similarly demonstrate peripheral enhancement and central non-enhancement during the arterial phase, followed by washout in subsequent venous and delayed phases, along with distortion of the renal vasculature and calyces giving a picture of renal metastasis (Fig. 2 B).

Furthermore, the liver exhibits heterogeneously enhancing intraparenchymal hypodense lesions, suggesting hepatic secondaries (Fig. 2 A). Thorax exhibits multiple enhancing soft tissue dense nodules involving bilateral lung fields, with bilateral mild pleural effusion, suggesting pulmonary secondaries (Fig. 3).

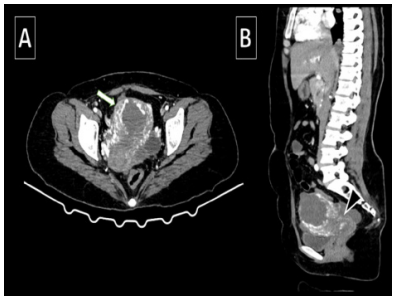

Fig. 1 A/B: (A) CECT abdomen and pelvis, axial section showing mixed-dense lesion located within the myometrium of the fundus of the uterus, causing contour bulge and effacing the zonal anatomy of the uterine parenchyma, post-contrast imaging of this lesion highlights peripheral intensely enhancing serpiginous features (White arrow). (B) CECT abdomen and pelvis, sagittal section showing multiple engorged, and tortuous enhancing Para uterine/gonadal vessels, along with focal enhancing nodular thickening affecting the anterior wall of the vagina, suggestive of vaginal extension of the lesion (Black arrow head).

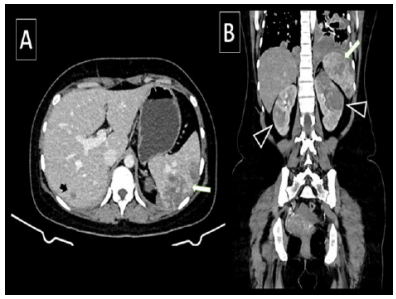

Fig. 2 A/B: (A) CECT abdomen and pelvis, axial section showing hypodense lesions within the spleen, which exhibit peripheral enhancement and central non-enhancement post contrast, suggesting splenic metastasis (White arrow), the liver exhibits heterogeneously enhancing intraparenchymal hypodense lesions, suggesting hepatic secondaries (Black arrow). (B) CECT abdomen and pelvis, coronal exhibits multiple iso - dense and mildly hyperdense lesions involving both cortical and medullary regions of both kidneys suggestive of renal secondaries (Black arrow head) and splenic secondaries (White arrow).

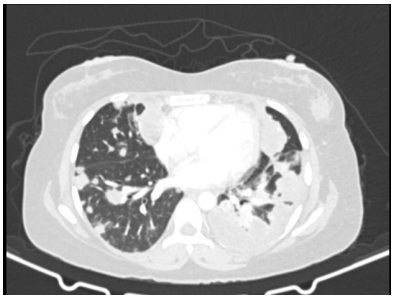

Fig.3: CECT thorax axial section demonstrates multiple enhancing soft tissue dense nodules involving bilateral lung fields, suggesting pulmonary secondaries.

Surgical intervention was deemed necessary due to the extent of metastasis. She underwent a total abdominal hysterectomy with bilateral salpingo-oophorectomy and resection of accessible metastases. Biopsy post-surgery was conclusive of choriocarcinoma, confirming the initial suspicion based on clinical and radiological findings.

Post-operative recovery was uneventful, and she was discharged with a plan for adjuvant chemotherapy regimen including a combination of methotrexate, etoposide, actinomycin-D, cyclophosphamide, and vincristine.In the first six months following surgery and initiation of adjuvant chemotherapy, she underwent regular follow-up visits every 4-6 weeks to monitor her clinical progress, despite initial resistance, subsequent imaging and β-hCG levels showed no evidence of recurrence, and the patient remains in remission. Her overall longevity has been extended, highlighting the effectiveness of the multidisciplinary treatment approach. Long-term follow-up is ongoing to monitor for late recurrences, complications from metastasis and manage any delayed treatment-related side effects.

DISCUSSION

Gestational trophoblastic neoplasia (GTN) encompasses a diverse spectrum of conditions arising from abnormal trophoblastic proliferation, with distinct clinical presentations and prognostic implications. The classification of GTN includes hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumour (PSTT), and epithelioid trophoblastic tumour (ETT) [4]. Hydatidiform mole is characterized by abnormal trophoblastic proliferation, whereas invasive mole exhibits infiltration of trophoblastic cells into the uterine wall. Choriocarcinoma represents the most aggressive form of GTN, characterized by malignant trophoblastic cells with potential for hematogenous dissemination. PSTT and ETT are rare variants of GTN, exhibiting distinct histological features and clinical behaviour. Classification is essential for guiding management decisions and predicting treatment outcomes, emphasizing the importance of accurate histopathological evaluation and comprehensive staging in patients with GTN.

Common clinical manifestations of GTN include vaginal bleeding, which may range from spotting to profuse haemorrhage, along with uterine enlargement and abnormal uterine bleeding patterns [1, 2]. Additionally, patients may experience symptoms such as pelvic pain or discomfort, dyspnoea, and symptoms suggestive of metastatic spread, including cough, haemoptysis, and neurologic deficits [4]. Several risk factors predispose individuals to GTN, including advanced maternal age, multiparity, prior history of molar pregnancy or miscarriages, and ethnic predisposition [2]. Furthermore, certain genetic predispositions and environmental factors may contribute to the development of GTN, highlighting the importance of comprehensive risk assessment and vigilant monitoring in at-risk populations.

Management of GTN involves a multimodal approach, incorporating chemotherapy, surgery, and supportive care. Chemotherapy regimens typically include a combination of agents such as methotrexate, etoposide, actinomycin-D, and cisplatin (MEP-CA). This combination was selected based on its efficacy in treating high-risk GTN, leveraging multiple mechanisms of action to target rapidly proliferating trophoblastic cells [5]. Methotrexate inhibits folic acid metabolism, etoposide disrupts DNA synthesis, actinomycin-D intercalates DNA, cyclophosphamide alkylates DNA, and vincristine inhibits microtubule formation, collectively enhancing therapeutic effectiveness [5]. While chemotherapy is effective in inducing remission in the majority of GTN cases, refractory disease or metastatic spread may necessitate surgical intervention [5]. The rationale for choosing this surgical approach was based on the extent of metastasis and the need to remove as much tumour burden as possible, thereby enhancing the effectiveness of subsequent chemotherapy. However, the optimal treatment approach may vary depending on factors such as the histological subtype, stage of disease, and patient preferences. In our case, the patient underwent a comprehensive treatment strategy encompassing surgical resection of the primary neoplasm followed by chemotherapy.

Prognostic indicators in gestational trophoblastic neoplasia (GTN) include factors such as the stage of the disease, the specific histological subtype, serum levels of beta-human chorionic gonadotropin (β-hCG), and the patient's response to treatment [2]. Conditions considered high-risk, like widespread metastases and resistance to chemotherapy, suggest a more unfavourable outlook and may necessitate aggressive treatment strategies and vigilant monitoring. In this case, the high β-hCG levels, extensive metastatic spread to multiple organs, and initial chemotherapy resistance were significant negative prognostic factors, indicating advanced disease and a challenging treatment course. Conversely, the patient's young age and good performance status were favourable prognostic factors, enhancing her ability to tolerate aggressive treatments and improving

recovery prospects. These mixed prognostic signals necessitated a highly tailored and intensive treatment strategy, combining surgical intervention and a robust chemotherapy regimen. Continuous monitoring and adaptive treatment adjustments were essential in managing the disease's progression and optimizing the patient's overall outcome.

Our case highlights the challenges inherent in managing advanced GTN with multifocal metastatic involvement and also highlights the contributions of various specialties in managing advanced GTN. The gynaecologic oncology team performed the surgical resection, while the medical oncology team managed the chemotherapy regimen. Radiologists played a crucial role in diagnosing and monitoring the extent of metastasis through imaging studies. The pathology team confirmed the diagnosis through histological analysis. Supportive care from nursing staff and the involvement of a nutritionist helped manage treatment side effects and improve the patient's overall well-being. This collaborative approach was vital for optimizing patient outcomes.

CONCLUSION

In summary, the case of a 26-year-old female with multifocal metastatic gestational trophoblastic neoplasia (GTN) underscores the challenges in its diagnosis and management. Despite aggressive treatment, including chemotherapy and multidisciplinary care, the patient showed resistance and persistent metastases, highlighting the aggressiveness of advanced GTN. Early recognition, comprehensive staging, and tailored treatment strategies are crucial for optimizing outcomes in GTN patients. Further research is essential to advance therapeutic approaches and improve patient prognosis.

Special thanks to Dr. Paarthipan Natarajan, Professor and Head of the Department of Radiology at Saveetha Medical College, for his invaluable guidance and insights throughout this case report. His expertise and mentorship have been instrumental in shaping our understanding of radiological aspects and enhancing the quality of this work. We deeply appreciate his support and contribution to our academic endeavours.

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